I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Decisions & Certifications of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: April 16, 2008 Signature: (Mary Jane DiPalma)

Docket No.: JHUC-P01-016 (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of:
Beachy et al.

Art Unit: 1623

Patent No.: 7,098,196

Examiner: Lewis, Patrick, T.

Issued: August 29, 2006

Confirmation No.: 8453

For: MEDIATORS OF HEDGEHOG SIGNALING PATHWAYS, COMPOSITIONS AND USES RELATED THERETO

REQUEST FOR RECONSIDERATION OF CERTIFICATE OF CORRECTION

Decisions & Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In reply to the Patent Office notice regarding Request for Certificate of Correction mailed on November 15, 2006, Applicants respectfully request reconsideration of the Request for Certificate of Correction that was filed on October 17, 2006.

Enclosed are copies of the Request for Certificate of Correction, Certificate of Correction, the Examiner's Amendment mailed on September 27, 2005 and the Reply filed on August 3, 2005 which evidences the Patent Office error, and the PTO stamped returned postcard for the Reply.

Please note claim 1 of our Reply (page 4, lines 11-12) states $-(CH_2)-R_8$.

Further, please note claim 3 of our Reply (page 6, lines 9-10) states $-(CH_2)-R_8$.

Finally, please note the Examiners amendment states in claims 3, lines 23-24, the text "and either R_6 and R_7, or" was deleted.

In view of the above evidence which has been highlighted on the respective documents, kindly issue a Certificate of Correction as noted on the attached PTO Form SB/44.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JHUC-P01-016 from which the undersigned is authorized to draw.

Dated: April 16, 2008

Respectfully submitted,

By _____
David P. Halstead, Ph.D.
Registration No.: 44,735
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Attention: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: October 17, 2006 Signature: (Mary Jane DiPalma)

Docket No.: JHUC-P01-016
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of:
Beachy et al.

Patent No.: 7,098,196

Issued: August 29, 2006

For: REGULATORS OF THE HEDGEHOG PATHWAY, COMPOSITIONS AND USES RELATED THERETO

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.322

Attention: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted typographical errors which should be corrected.

In the Claims:

In Claim 1, col. 135, line 52, change "or (CH_2)-R_8" to --or -(CH_2)-R_8--;

Claim 3, col. 137, line 7, change "or (CH_2)-R_8" to --or -(CH_2)-R_8--; and

Claim 3, col. 137, line 25, delete "R_7, or".

The errors were not in the application as filed by applicant; accordingly no fee is required.

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Patentee respectfully solicits the granting of the requested Certificate of Correction.

Applicant believes no fee is due with this request. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JHUC-P01-016 from which the undersigned is authorized to draw.

Dated: October 17, 2006

Respectfully submitted,

By

David P. Halstead, Ph.D.
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FISH & NEAVE IP GROUP, ROPES & GRAY LLP
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Attorneys/Agents For Applicant

PTO/SB/44 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO.	:	7,098,196
APPLICATION NO.	:	09/688,076
ISSUE DATE	:	August 29, 2006
INVENTOR(S)	:	Beachy et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the claims:

Claim 1, col. 135, line 52, change "or (CH_2)-R_6" to --or -(CH_2)-R_6--;

Claim 3, col. 137, line 7, change "or (CH_2)-R_6" to --or -(CH_2)-R_6--; and

Claim 3, col. 137, line 25, delete "R_7, or".

MAILING ADDRESS OF SENDER (Please do not use customer number below):
David P. Halstead, Ph.D.
FISH & NEAVE IP GROUP, ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624

Via: ss Mail	Atty Dkt No.: JHUC-P01-016
Inventor: Beachy et al.	
Application No.: 09/688076	Filing Date: October 13, 2000
Title: REGULATORS OF THE HEDGEHOG PATHWAY, COMPOSITIONS AND USES RELATED THERETO	

Documents Filed:
Amendment and Reply under 37 CFR section 1.116 (26 pages)

Return receipt postcard

Sender's Initials: JKH/CAM/jlm	Date: August 3, 2005

9786946_1.DOC

Via: First Class Mail	Atty Dkt No.: JHUC-P01-016
Inventor: Beachy et al.	
Application No.: 09/688076	Filing Date: October 13, 2000
Title: REGULATORS OF THE HEDGEHOG PATHWAY, COMPOSITIONS AND USES RELATED THERETO	

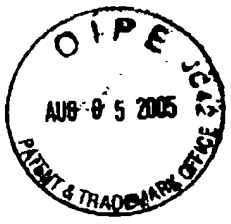
Documents Filed:
Amendment and Reply under 37 CFR section 1.116 (26 pages)

Return receipt postcard

Ropes & Gray

AUG 10 2005

Intellectual Property Dept.



Sender's Initials: JKH/CAM/jlm	Date: August 3, 2005

9786946_1.DOC

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: MS AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: August 3, 2005 Signature: Jodi Lee Mullins

Docket No.: JHUC-P01-016 (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Beachy, et al.

Application No.: 09/688,076 Confirmation No.: 8453

Filed: October 13, 2000 Art Unit: 1623

For: REGULATORS OF THE HEDGEHOG PATHWAY, COMPOSITIONS AND USES RELATED THERETO Examiner: LEWIS, Patrick T.

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND REPLY UNDER 37 CFR § 1.116

Sir:

This Reply is being filed in reply to the outstanding Final Office Action, mailed May 5, 2005 in connection with the above application. Please enter the following amendments:

IN THE SPECIFICATION:

On page 34, please amend the last paragraph as follows:

R_2[[,]] and R_3~~, R_4, and R_5~~ represent one or more substitutions to the ring to which each is attached, for each occurrence, independently represent hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar (e.g., monosaccharide, disaccharide, polysaccharide, etc.), carbamate (e.g., attached to the steroid at oxygen), carbonate, or $-(CH_2)_m-R_8$;

R_4 and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or $-(CH_2)_m-R_8$;

On page 36, after the paragraph ending in "...pyridazine, etc." please insert the following paragraph:

In certain embodiments, R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy; R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; and R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

On page 38, after the paragraph ending in "...non-hydrogen atoms," please insert the following paragraph:

In certain embodiments, R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy; R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; R_4, for each

occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

On page 40, after the paragraph ending in "...non-hydrogen atoms," please insert the following paragraph:

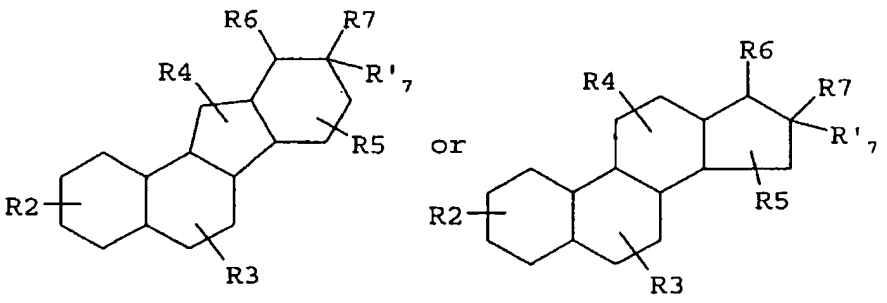
In certain embodiments, R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy; R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

On page 42, after the paragraph ending in "...non-hydrogen atoms," please insert the following paragraph:

In certain embodiments, R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy; R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

IN THE CLAIMS:

1. (currently amended) A compound represented in the general formulas (I), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula I

wherein, as valence and stability permit,

R_2[[,]] and R_3, ~~R_4, and R_5,~~ independently for each occurrence, ~~are absent or~~ represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, ~~or~~ ~~$(CH_2)_m$-R_8~~;

R_4 and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or -$(CH_2)_m$-R_8;

R_6, R_7, and R'_7, are absent or represent, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether,

thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$, and

either R_6 and R_7, or R_7 and R'_7, taken together, form a substituted or unsubstituted ring or polycycle, which includes a tertiary amine in the atoms which make up the ring, wherein, if the ring is formed by R_7 and R'_7, the tertiary amine contained therein is substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle; and

m is an integer in the range 0 to 8 inclusive;

or a pharmaceutically acceptable salt thereof.

2. (original) The compound of claim 1, wherein:

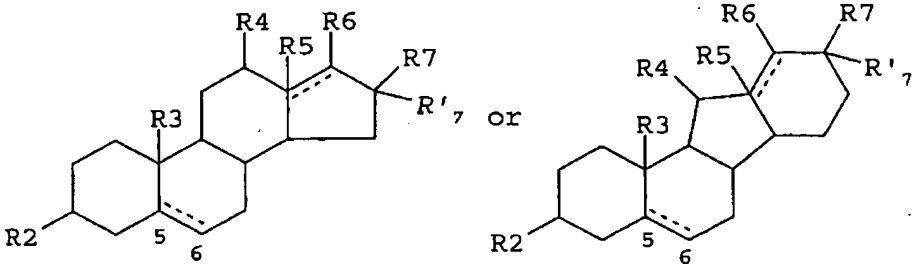
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$;

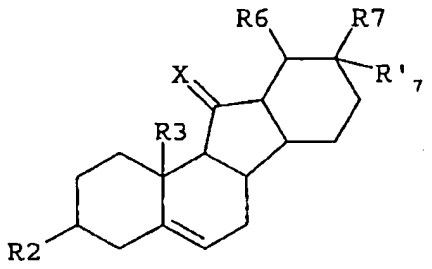
R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

3. (currently amended) A compound represented in the general formula (II), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



or



Formula II

wherein, as valence and stability permit,

R_2[[,]] and R_3, ~~R_4, and R_5~~, independently for each occurrence, ~~are absent or~~ represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, ~~or~~ $(CH_2)_m$-R_8;

R_4 and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or -$(CH_2)_m$-R_8;

R_6, R_7, and R'_7, are absent or represent, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or -$(CH_2)_m$-R_8, and

either R_6 and R_7, or R_7 and R'_7, taken together, form a substituted or unsubstituted ring or polycycle, ~~and~~ which includes a tertiary amine in the atoms which make up the ring, wherein, if the ring is formed by R_7 and R'_7, the tertiary amine contained therein is

substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

X represents O or S; and

m is an integer in the range 0 to 8 inclusive;

or a pharmaceutically acceptable salt thereof.

4. (original) The compound of claim 3, wherein:

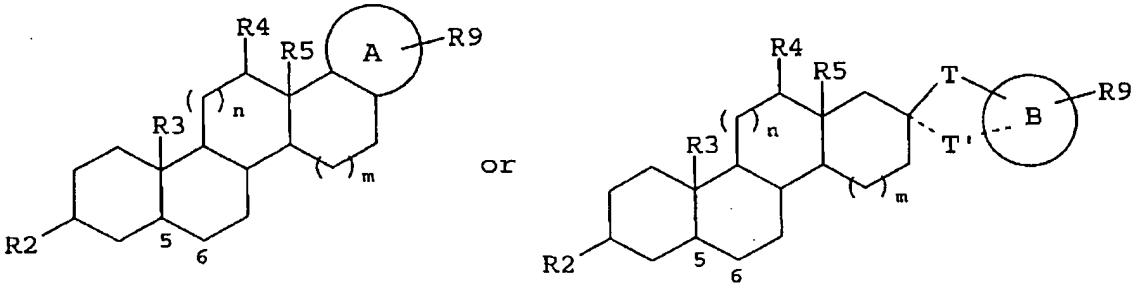
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

5. (currently amended) A compound represented in the general formula (III), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula III

wherein, as valence and stability permit,

R_2[[,]] and R_3, ~~R_4, and R_5,~~ independently for each occurrence, ~~are absent or~~ represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls,

carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or -$(CH_2)_m$-R_8;

R_4 and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or -$(CH_2)_m$-R_8;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

A and B represent monocyclic or polycyclic groups;

T represents an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-10 bond lengths;

T' is absent, or represents an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-3 bond lengths, wherein if T and T' are both present, T and T' taken together with the ring B form a covalently closed ring of 5-8 ring atoms;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or -$(CH_2)_m$-R_8; and

n and m are, independently, zero, 1 or 2;

with the proviso that A, or T, T', and B, taken together, include at least one tertiary amine;

wherein the tertiary amine is substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl;

or a pharmaceutically acceptable salt thereof.

6. (original) The compound of claim 5, wherein:

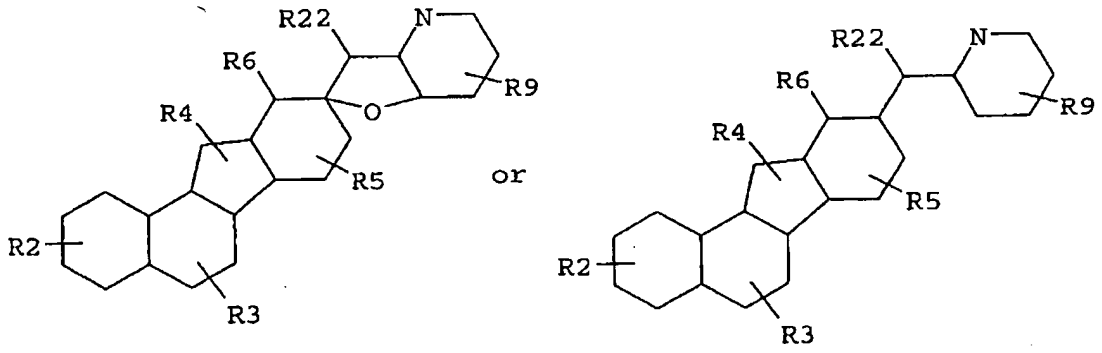
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

7. (currently amended) A compound represented in the general formula (IV), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula IV

wherein, as valence and stability permit,

R_2[[,]] and R_3, ~~R_4, and R_5,~~ independently for each occurrence, ~~are absent or~~ represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or -$(CH_2)_m$-R_8;

R_4 and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides,

anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or -$(CH_2)_m$-R_8;

R_6 is absent or represents, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or -$(CH_2)_m$-R_8;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or -$(CH_2)_m$-R_8;

R_{22} is absent or represents an alkyl, an alkoxyl or –OH; and

m is an integer in the range 0 to 8 inclusive,

wherein at least one occurrence of R_9 is bound to N, thereby forming a tertiary amine, and this occurrence of R_9 is an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl; or a pharmaceutically acceptable salt thereof.

8. (original) The compound of claim 7, wherein:

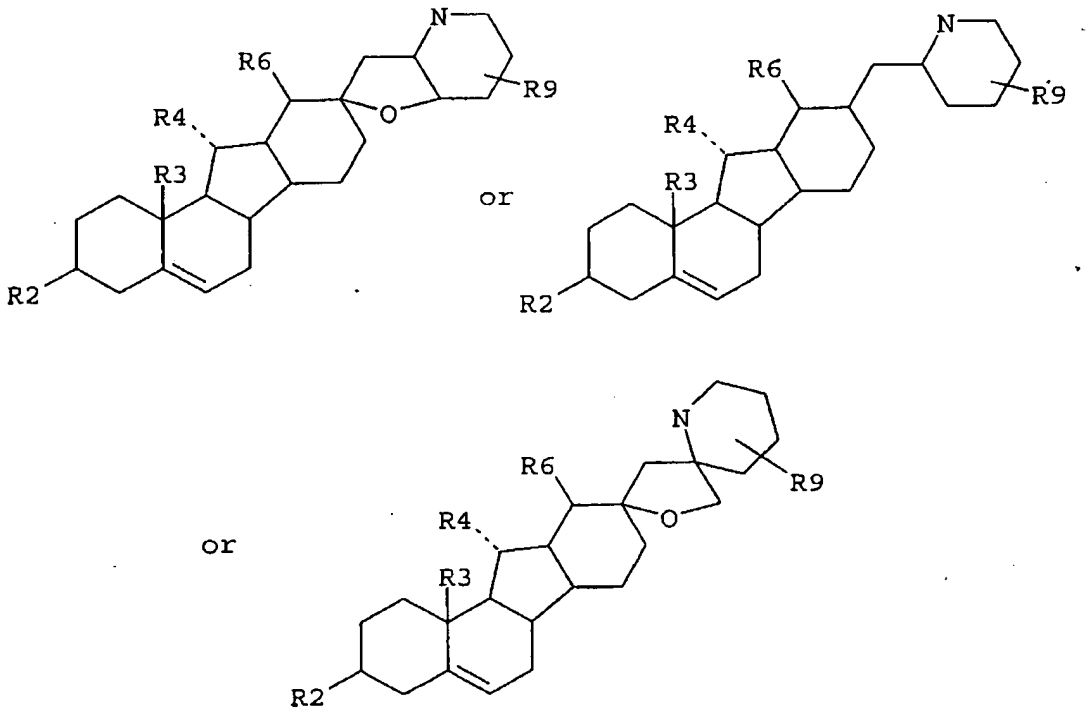
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

9. (currently amended) A compound represented in the general formula (V) or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula V

wherein, as valence and stability permit,

R_2[[,]] and R_3, ~~and R_4~~, independently for each occurrence, ~~are absent or~~ represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or $-(CH_2)_m-R_8$;

R_4 is absent or represents one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate carbonate, or $-(CH_2)_m-R_8$;

R_6 is absent or represents halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$; and

m is an integer in the range 0 to 8 inclusive,

wherein at least one occurrence of R_9 is attached to N, thereby forming a tertiary amine, and this occurrence of R_9 is an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ketone, ether, halogen, alkenyl, and alkynyl;

or a pharmaceutically acceptable salt thereof.

10. (currently amended) The compound of claim 9, wherein:

R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; ~~and~~

~~R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl~~.

11. (withdrawn) A method for treating basal cell carcinoma, comprising administering to a patient a compound of any of claims 1-10.

12. (withdrawn) The method of claim 11, wherein the compound is administered locally to a tumor.

13. (withdrawn) A method for regulating differentiation or proliferation of a cell, comprising administering to a patient a compound of any of claims 1-10.

14. (withdrawn) A method for controlling the growth or development of pancreatic tissue, comprising contacting the tissue with a compound of any of claims 1-10.

15. (withdrawn) A method for treating medulloblastoma, comprising administering to a patient a compound of any of claims 1-10.

16. (withdrawn) The method of claim 15, wherein the compound is administered locally to a tumor.

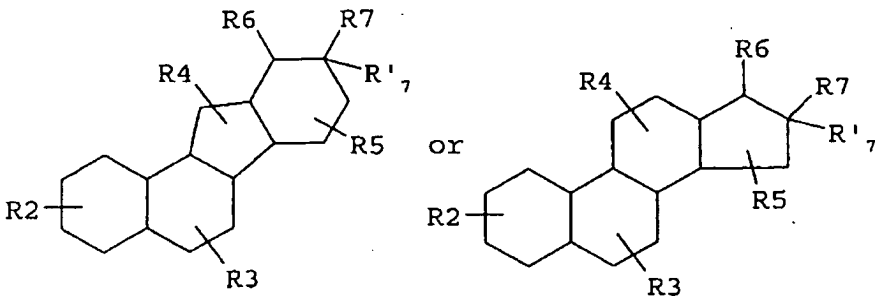
17. (withdrawn) A method for treating a hyperproliferative disorder, comprising administering to a patient a compound of any of claims 1-10.

18. (withdrawn) The method of claim 17, wherein the compound is administered topically.

19. (withdrawn) The method of claim 17, wherein the compound is administered locally.

20. (original) A pharmaceutical preparation comprising a compound of any of claims 1-10 and a pharmaceutically acceptable excipient.

21. (withdrawn) A method for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a steroidal alkaloid represented in the general formulas (I), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula I

wherein, as valence and stability permit,

R_2, R_3, R_4, and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or $-(CH_2)_m-R_8$;

R_6, R_7, and R'_7, are absent or represent, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$, and

either R_6 and R_7, or R_7 and R'_7, taken together, form a substituted or unsubstituted ring or polycycle, which includes a tertiary amine in the atoms which make up the ring, wherein, if the ring is formed by R_7 and R'_7, the tertiary amine contained therein is substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle; and

m is an integer in the range 0 to 8 inclusive.

22. (withdrawn) The method of claim 21, wherein:

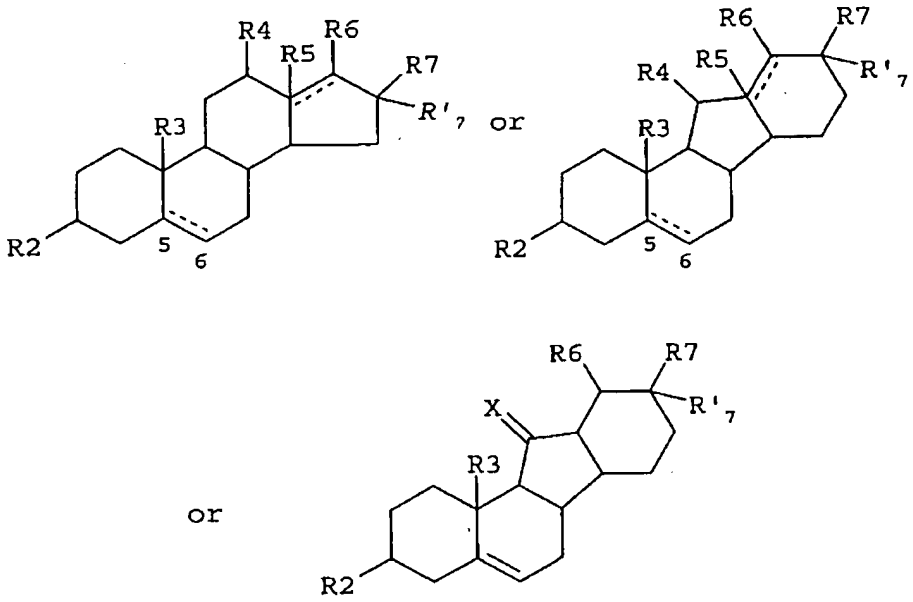
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

23. (withdrawn) A method for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a steroidal alkaloid represented in the general formula (II), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula II

wherein, as valence and stability permit,

R_2, R_3, R_4, and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls,

carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or $-(CH_2)_m-R_8$;

R_6, R_7, and R'_7, are absent or represent, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$, and

either R_6 and R_7, or R_7 and R'_7, taken together, form a substituted or unsubstituted ring or polycycle, which includes a tertiary amine in the atoms which make up the ring, wherein, if the ring is formed by R_7 and R'_7, the tertiary amine contained therein is substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

X represents O or S; and

m is an integer in the range 0 to 8 inclusive.

24. (withdrawn) The method of claim 23, wherein:

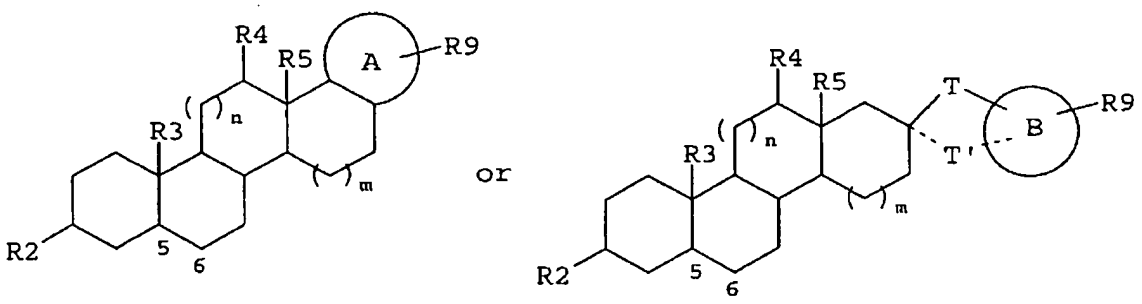
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

25. (withdrawn) A method for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a steroidal alkaloid represented in the general formula (III), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula III

wherein, as valence and stability permit,

R_2, R_3, R_4, and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, sugar, carbamate, carbonate, or $-(CH_2)_m-R_8$;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

A and B represent monocyclic or polycyclic groups;

T represents an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-10 bond lengths;

T' is absent, or represents an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, ether or amine linkage of 1-3 bond lengths, wherein if T and T' are both present, T and T' taken together with the ring B form a covalently closed ring of 5-8 ring atoms;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$; and

n and m are, independently, zero, 1 or 2;

with the proviso that A, or T, T', and B, taken together, include at least one tertiary amine;

wherein the tertiary amine is substituted by an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl.

26. (withdrawn) The method of claim 25, wherein:

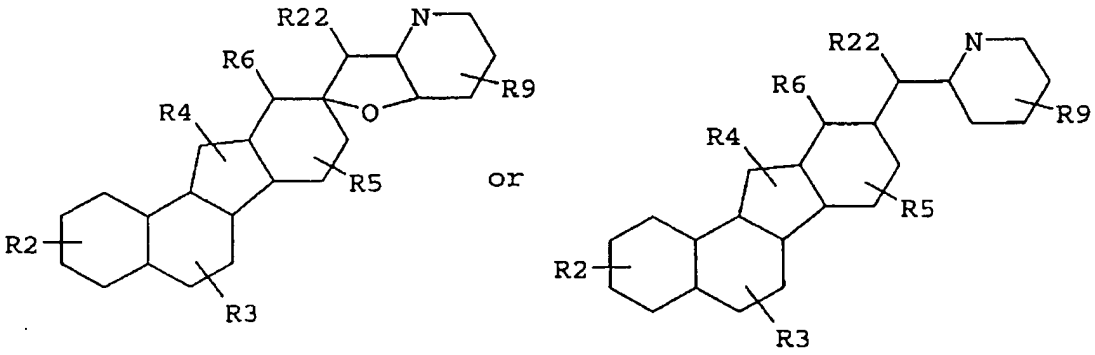
R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or -C(O)-R_8; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

27. (withdrawn) A method for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell with a steroidal alkaloid represented in the general formula (IV), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula IV

wherein, as valence and stability permit,

R_2, R_3, R_4, and R_5, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls,

carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or $-(CH_2)_m-R_8$;

R_6 is absent or represents, independently, halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$;

R_{22} is absent or represents an alkyl, an alkoxyl or –OH; and

m is an integer in the range 0 to 8 inclusive,

wherein at least one occurrence of R_9 is bound to N, thereby forming a tertiary amine, and this occurrence of R_9 is an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl.

28. (withdrawn) The method of claim 27, wherein:

R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

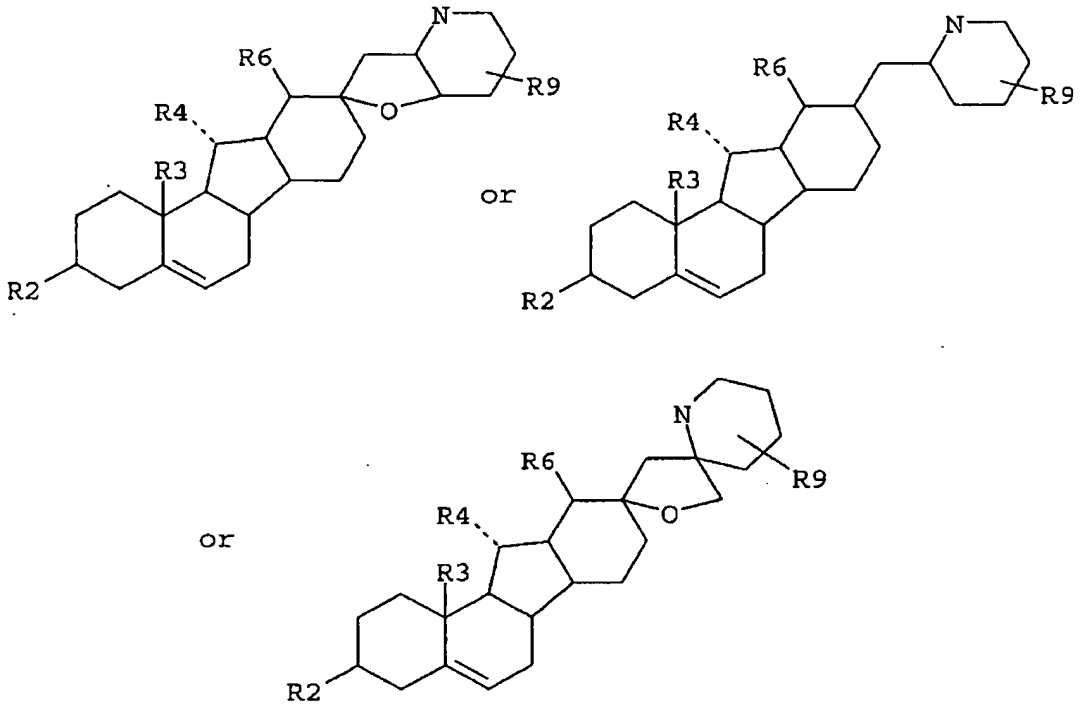
R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

29. (withdrawn) A method for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of-function phenotype or a *smoothened* gain-of-function phenotype, comprising contacting the cell

with a steroidal alkaloid represented in the general formula (V) or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



Formula V

wherein, as valence and stability permit,

R_2, R_3, and R_4, independently for each occurrence, are absent or represent one or more substitutions to the ring to which each is attached, selected from hydrogen, halogens, alkyls, alkenyls, alkynyls, aryls, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amines, imines, amides, phosphoryls, phosphonates, phosphines, carbonyls, carboxyls, carboxamides, anhydrides, silyls, ethers, thioethers, alkylsulfonyls, arylsulfonyls, selenoethers, ketones, aldehydes, esters, or $-(CH_2)_m-R_8$;

R_6 is absent or represents halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$;

R_8 represents an aryl, a cycloalkyl, a cycloalkenyl, a heterocycle, or a polycycle;

R_9 is absent or, independently for each occurrence, represents one or more substitutions to the ring to which it is attached, selected from halogen, alkyl, alkenyl, alkynyl, aryl, hydroxyl, =O, =S, alkoxyl, silyloxy, amino, nitro, thiol, amine, imine, amide, phosphoryl, phosphonate, phosphine, carbonyl, carboxyl, carboxamide, anhydride, silyl, ether, thioether, alkylsulfonyl, arylsulfonyl, selenoether, ketone, aldehyde, ester, or $-(CH_2)_m-R_8$; and

m is an integer in the range 0 to 8 inclusive,

wherein at least one occurrence of R_9 is attached to N, thereby forming a tertiary amine, and this occurrence of R_9 is an alkyl substituted with a group selected from aryl, aralkyl, heteroaryl, heteroaralkyl, amide, acylamino, carbonyl, ester, carbamate, urea, ketone, sulfonamide, carbocyclyl, heterocyclyl, polycyclyl, ether, halogen, alkenyl, and alkynyl.

30. (withdrawn) The method of claim 29, wherein:

R_2 represents =O, sugar, carbamate, ester, carbonate, or alkoxy;

R_3, for each occurrence, is an -OH, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$;

R_4, for each occurrence, is absent, or represents -OH, =O, alkyl, -O-alkyl, -C(O)-alkyl, or $-C(O)-R_8$; and

R_5, for each occurrence, is absent, or represents -OH, =O, or alkyl.

31. (withdrawn) The method of any of claims 21-30, wherein the tertiary amine includes a hydrophobic extraannular substituent.

32. (withdrawn) The method of claim 31, wherein the hydrophobic extraannular substituent includes an aryl, heteroaryl, carbocyclyl, heterocyclyl, or polycyclyl group.

33. (withdrawn) The method of claim 32, wherein the hydrophobic extraannular substituent includes a polycyclyl group selected from biotin, a zwitterionic complex of boron, and a steroidal polycycle.

34. (withdrawn) The method of claim 31, wherein the hydrophobic substituent consists essentially of a combination of alkyl, amido, acylamino, ketone, ester, ether, halogen, alkenyl, alkynyl, aryl, aralkyl, urea, or similar functional groups, including between 5 and 40 non-hydrogen atoms.

35. (withdrawn) The method of any of claims 21-30, wherein the steroidal alkaloid inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED_{50} of 1 mM or less.

36. (withdrawn) The method of any of claims 21-30, wherein the steroidal alkaloid inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED_{50} of 1 μM or less.

37. (withdrawn) The method of any of claims 21-30, wherein the steroidal alkaloid inhibits *ptc* loss-of-function or *smoothened* gain-of-function mediated signal transduction with an ED_{50} of 1 nM or less.

38. (withdrawn) The method of any of claims 21-30, wherein the cell is contacted with the steroidal alkaloid *in vitro*.

39. (withdrawn) The method of any of claims 21-30, wherein the cell is contacted with the steroidal alkaloid *in vivo*.

40. (withdrawn) The method of any of claims 21-30, wherein the steroidal alkaloid is administered as part of a therapeutic or cosmetic application.

41. (withdrawn) The method of claim 40, wherein the therapeutic or cosmetic application is selected from the group consisting of regulation of neural tissues, bone and cartilage formation and repair, regulation of spermatogenesis, regulation of smooth muscle, regulation of lung, liver and other organs arising from the primitive gut, regulation of hematopoietic function, and regulation of skin and hair growth.

42. (cancelled)

REMARKS

Following entry of the foregoing amendments, claims 1-41 constitute the pending claims in the present application. Claims 11-19 and 21-41 are withdrawn from consideration. Claims 1-10, 20, and 42 stand rejected. Claims 1, 3, 5, 7, 9, and 10 are currently amended. Claim 42 is cancelled.

Applicants respectfully request reconsideration in view of the amendments made herein and the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1-3. Election/Restrictions

The Examiner has withdrawn from consideration claims 11-19 and 21-41 as being drawn to non-elected inventions. As acknowledged by the Examiner, Applicants timely traversed the restriction requirement in their Reply mailed July 23, 2003. In particular, in their Reply to the Restriction Requirement Applicants requested rejoinder of the claims of Group V (claims 1-10, 20, and 42) and Group XI (claims 11-19) and illustrated that a search of the compounds of Group V would necessarily encompass a search of the methods of using such compounds, i.e. Group XI, while presenting no additional burden on the Examiner.

Nevertheless, pursuant to MPEP 809: "Any claim(s) directed to the nonelected invention(s), previously withdrawn from consideration, which depends from or includes all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability." Accordingly, although the restriction has been made final, Applicants note that on indication of allowance of generic/linking claims 1-10, dependent claims 11-19 must be rejoined and fully examined; that is, when a generic claim is found allowable, "applicant must be advised of the allowable generic claim and that claims drawn to the nonelected species are no longer withdrawn since they are fully embraced by the allowed generic claim" (MPEP 809.02(c)).

Furthermore, in accordance with MPEP 821.04, in cases where claims to a product and a process for making or using the product are presented in the same application, "if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined." See *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995). As such, on indication of allowance of product claims 1-10, Applicants note that

rejoinder of process claims 11-19, which depend from and include all the limitations of claims 1-10, is required as a matter of right (MPEP 821.04).

4-5. Withdrawal of Objections

Applicants note with appreciation the withdrawal of objections of claims 2, 4, 6, 8, and 10 under 37 CFR 1.75(c).

6. Withdrawal of Rejections – 35 USC 102

Applicants note with appreciation the withdrawal of rejections of claims 1-10 under 35 USC 102(b) over Suginome *et al. Bull. Chem. Soc. Jpn.* **1981**, *54*, 3042-3047 ("Suginome").

7. Withdrawal of Rejections – 35 USC 103

Applicants note with appreciation the withdrawal of rejections of claims 1-10 under 35 USC 103(a) over Suginome.

8-9. Claim Rejections – 35 USC 112, First Paragraph

Claims 1-10, 20, and 42 are rejected under 35 USC, first paragraph, as failing to comply with the written description requirement. Applicants appreciate the Examiner's helpful suggestions in the telephonic discussion of July 12, 2005. Accordingly, the specification and the pending claims are amended as suggested by the Examiner to address the present written description rejection.

Claims 1, 3, 5, 7, and 9 are amended to recite that R4 and R5 may be absent and to delete the option that R2 and R3 are absent. Support for R4 being absent in Formulas I, II, III, IV, and V can be found in the specification on page 35, last full paragraph; page 37, second paragraph; page 39, second paragraph; page 41, third paragraph; and page 43, first paragraph, respectively. Support for R5 being absent in Formulas I, II, III, IV, and V can be found in the disclosure in originally filed claims 2, 4, 6, and 8, respectively. Additionally, the specification is hereby amended to incorporate matter from original claims 2, 4, 6, and 8. As such, Applicants assert that the instant amendments to claims 1, 3, 5, 7, and 9 present no new matter and overcome the outstanding written description rejection. Since claims 2, 4, 6, 8, 10, and 20 depend directly or indirectly from claims 1, 3, 5, 7, and 9, Applicants assert these claims also overcome the present rejection. Reconsideration and withdrawal of the rejection is respectfully requested. Claim 42 is cancelled rendering the rejection over this claim moot.

Additional Claim Amendments

Claims 1, 3, 5, 7, and 9 are amended to recite "pharmaceutically acceptable salts" of the compounds therein. Support for these amendments can be found in the specification, for example from page 79, first full paragraph to page 80, first full paragraph. Claim 10 is amended to correct matters of form. These amendments present no new matter.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Dated: August 3, 2005

Respectfully submitted, Reg No. 44,778

By Jennifer Gelman for
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Attorneys/Agents For Applicant

EXAMINER'S AMENDMENT

1. Claims 1-10 and 20 are directed to an allowable product. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims 11-12 and 15-16, directed to the process of making or using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, are now subject to being rejoined. Claims 11-12 and 15-16 are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Since all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, the restriction requirement made in the Office action mailed on June 23, 2003 is hereby withdrawn.

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David Halstead on September 13, 2005.

The application has been amended as follows:

In claim 1, lines 22-23, the text "and either R_6 and R_7, or" has been deleted.

In claim 3, lines 23-24, the text "and either R_6 and R_7, or" has been deleted.

In claim 5, line 3, the chemical structure on the left which incorporates Ring A and the term "or" have been deleted; line 19, the text "A and B represent monocyclic or polycyclic groups" has been deleted and the text —B represents a monocyclic or

polycyclic group--- has been inserted therefor; line 32, the term "A, or" has been deleted.

In claim 7, line 22, the phrase "absent or," has been deleted.

In claim 9, line 24, the phrase "absent or," has been deleted.

Claims 13-14, 17-19 and 21-41 have been canceled.

Reasons for Allowance

3. The following is an examiner's statement of reasons for allowance:

Suginome et al. Bull. Chem. Soc. Jpn., (1981), Vol. 54, pages 3042-3047 (Suginome) is the closest prior art. Suginome discloses the oxidized derivative of N-acetyljervine, compound **3** (Scheme 1, page 3043). Compound **3** reads upon compounds wherein R_2 is =O, R_3 is CH_3, R_4 is =O, R_5 is H or not present, R_6 is CH_3, and R_7 and R'_7 are taken together to form a polycycle which includes a tertiary amine in the atoms which make up the ring. Suginome differs from the instantly claimed invention in that Suginome does not teach or suggest a compound wherein R_7 and R'_7 are taken together to form a polycycle which includes a tertiary amine in the atoms which make up the ring wherein the tertiary amine is substituted by an substituted alkyl.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

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